

HISTORY OF MEDICINE

Darwin's illness revealed

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After returning from the *Beagle* in 1836, Charles Darwin suffered for over 40 years from long bouts of vomiting, gut pain, headaches, severe tiredness, skin problems, and depression. Twenty doctors failed to treat him. Many books and papers have explained Darwin's mystery illness as organic or psychosomatic, including arsenic poisoning, Chagas' disease, multiple allergy, hypochondria, or bereavement syndrome. None stand up to full scrutiny. His medical history shows he had an organic problem, exacerbated by depression. Here we show that all Darwin's symptoms match systemic lactose intolerance. Vomiting and gut problems showed up two to three hours after a meal, the time it takes for lactose to reach the large intestine. His family history shows a major inherited component, as with genetically predisposed hypolactasia. Darwin only got better when, by chance, he stopped taking milk and cream. Darwin's illness highlights something else he missed—the importance of lactose in mammalian and human evolution.

diagnosis defied the 20 doctors, including his father, who examined him. Darwin's symptoms match exactly those we have described for systemic lactose intolerance.^{17–18} He only got better when, by chance, he reduced his milk and cream intake.

DARWIN'S ILLNESS

Charles Darwin recorded his symptoms and his tribulations in his health diary:

- Chronic fatigue and exhaustion
- Severe gastrointestinal problems, including pain
- Nausea
- Frequent vomiting
- A swimming head
- Severe headaches
- Trembling
- Insomnia
- Joint pain
- Rashes and eczema
- Mouth ulcers
- Boils
- Tooth and gum problems
- Heart palpitations
- Poor resistance to infections
- Depression.

His son Francis Darwin (1848–1925) wrote: "For nearly 40 years he never knew one day of the health of ordinary men, and his life was one long struggle against the weariness of strain and sickness".^{2–27} To see how this ill health affected Darwin you simply have to read the many letters to friends and family complaining of how unwell he felt all the time, and how it was slowing down his work.^{1–27} One year after returning from the *Beagle* voyage stress had an important effect on his overall wellbeing,^{15–16} and within another year he had given up going to parties. Some authors²⁹ have hinted that he didn't turn up to events because he was afraid to meet his critics face to face. But his letters¹ show that it was his illness that stopped from going to the famous Oxford debate in 1860, where Bishop Wilberforce (1805–1873) was confronted so successfully by T H Huxley (1825–1895). However, the real reason was his continuous ill health confining him to Down House. His friends had to come there to see him.

Attempts to unravel what might have been wrong with Charles Darwin have been confused by several unanswered questions:

- Did Darwin only really suffer after the *Beagle* trip, or had he suffered since childhood?
- Is there any evidence of an inherited problem in the Darwin/Wedgwood dynasties? This has

"I have had a bad spell. Vomiting every day for eleven days, and some days after every meal." Thus wrote Charles Darwin, aged 54, on 5 December 1863 to his friend Hooker.¹ For 40 years, Darwin suffered from a range of symptoms that devastated him for weeks on end. Explanations have been organic or psychosomatic (table 1).^{1–26} None have produced a satisfactory answer. On 10 December 1831, aged 22, Darwin was at Plymouth awaiting better weather for the *Beagle* to depart. To his horror he suffered a bout of the illness that was to plague him for the rest of his life (Darwin C R, *Diary of Health*, unpublished; Barlow *et al*²). He had chest pain and heart palpitations, but told no one at the time, fearing it might prevent him taking his trip of a lifetime. On the *Beagle* he seems to have been essentially healthy, apart from one bad bout of fever and frequent sea sickness. Returning home in 1836, he married in 1837 and set up house with Emma. On 20 September 1837, the problem struck again—heart palpitations. For the rest of his life he was to be plagued by ill health. Some bouts were so bad that, to his great frustration, he had to stop work for weeks. He recorded his symptoms in many letters and in his *Diary of Health*, which he wrote between 1 July 1849 and 16 January 1855. His worst problems were recurrent nausea, retching and vomiting, gut pain, flatulence, headaches, and a swimming head. He also suffered intermittently from eczema, particularly on the face, boils, and continual fatigue. No wonder he got depressed. The

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often been ignored because of lack of analysis of family records.

- How much did his medical history have an impact on his health? In particular did he have any severe illnesses as a child that could have left him with long term problems?
- Could he have poisoned himself with the chemicals used in his scientific work?
- When and why did his illness apparently abate towards the end of his life? This is important as there is no obvious reason for this if his problems were psychosomatic.

Several articles have claimed that Darwin (1809–1882) had excellent health at least until 1836, after the *Beagle*. Yet Darwin clearly described stomach pain, skin problems, mouth ulcers, and heart palpitations before this.^{1–2} He had scarlet fever at the age of 9, and notes excessive fatigue as early as 1829 at the age of 20. He had bouts of mouth sores and eczema while at Cambridge. And there was the heart palpitation incident that we described earlier as he waited to join the *Beagle* at Plymouth. This, with the family history,^{2–15–16–27–30} supports the hypothesis that the major cause of his symptoms, which became so bad in middle age, was both organic and hereditary. His seasickness on the *Beagle* is a red herring. He did have a major health crisis in Valparaíso in October 1834, leaving him ill in bed for more than a month. Several authors have concluded that this was a genuine organic illness, probably typhoid. Afterwards he complained of tiredness, and that small skin lesions tended to go septic. But despite these health problems, he did not suffer on the *Beagle* from the illness he complained of so much in later life.

Although his illustrious grandfather Erasmus Darwin (1731–1802) was a pioneer of immunisation, Charles was not immunised as we are today and was thus exposed to the usual set of 19th century childhood illnesses, including scarlet fever. He took a wide range of medications in an attempt to find a cure to his major problem. Darwin records taking several “poisons” as therapy throughout his life, including arsenic, bismuth, amyl nitrite, morphine, quinine, and calomel, which contains mercury. Many of these are known to have toxic side effects. Although the symptoms of arsenic poisoning bear some resemblance to Darwin's,¹⁴ they are not close enough. Furthermore, Darwin refused arsenic as a result of his father's advice. Scientists 150 years ago did not have to fill in COSHH forms. Darwin used many toxic chemicals in his study for fixing and preserving his specimens. These would have included phenol, formaldehyde, various alcohols, and stains. We have no way of knowing how exposure to these toxic chemicals affected Darwin's health. It would be surprising if they had no effect. There were many precedents of scientists poisoning themselves, including Humphry Davy (1778–1829) who almost certainly died of mercury poisoning, used for purifying the elements he discovered. However, the known toxic effects of the substances to which Darwin exposed himself cannot explain the breadth and timing of Darwin's organic symptoms.

Since Darwin's death there have been many attempts to explain his illness (table 1). Organic explanations include over 20 ailments, the most convincing being Chagas' disease.⁹ Chagas' disease is endemic in South America, and can be transmitted by the famous great bug of the Pampas, *Triatoma infestans*, a known carrier of *Trypanosoma cruzi*. Like *Giardia*, this protozoan infects the small intestine and other organs. Darwin describes being bitten by one of the great bugs in March 1834/5. But we now know that it is the excrement that carries the infectious agent. So how could cuts, abrasions, or bites in Darwin's skin have been exposed to this? The key is the description by Darwin that one of the officers on the *Beagle* kept a *Triatoma* as a pet, allowing it to feed on his blood. This would have left Darwin open to the excrement.

Table 1 Proposed causes of Darwin's disease

Causal type	Specific cause	Reference
Organic	Heart disease	Darwin himself (1831–1882) ^{1–2} and <i>Diary of Health</i> Obituary (1882) ² Obituary (1882) ⁴
	Nervous indigestion	
	Chronic from sea sickness	
	Chronic neurasthenia	Johnston, 1901 ⁵
	Chronic eye strain	Gould, 1903 ⁶
	Aftermath of Chilean fever	Leonard Huxley, 1927, see Colp ⁷
	Pyorrhoea	Leonard Darwin, 1927, see Colp ⁷
	Brucellosis	Simpson, 1958 ⁸
	Chagas' disease	Adler, 1959 ⁹
	Metabolic disease	Stetten, 1959 ¹⁰
	Acute intermittent porphyria	With, 1960, see King-Hele ¹¹
	Diaphragmatic hernia	Kohn, 1963 ¹²
	Narcolepsy (diabetes)	Roberts, 1966 ¹³
	Arsenic poisoning	Winslow, 1971 ¹⁴
	Pigeon allergy	Gruber and Barrett, 1974, see Colp ⁷
	Peptic ulcer	See Colp p130 ⁷
	Duodenal ulcer	See Colp p130 ⁷
	Appendicitis	see Colp p130 ⁷
	Smouldering hepatitis	See Colp p130 ⁷
	Cholecystitis	See Colp p130 ⁷
Psychosomatic	Amoeba infection	See Colp ⁷
	Allergy	Smith, 1990, 1992 ^{15–16}
	Systemic lactose intolerance	Campbell and Matthews, ^{17–18}
	1st psychoanalytical theory	Kemf, 1918 ¹⁹
	Hypochondria	Hubble, 1943 ²⁰
	Psychoneurosis	Hubble, 1943 ²⁰
	Chronic depression	Alvarez, 1959 ²¹
	Psychosomatic	Woodruff 1965 ²²
	Bereavement syndrome	Bolby, 1965, 1990 ^{23–24}
	Neurosis	Colp, 1977 ⁷
	Mixed psychosomatic	Colp, 1977 ⁷
	Anxiety state	Bernstein, 1982 ²⁵
	Panic syndrome	Barloon and Noyes, 1997 ²⁶

Any infection of the small intestine will cause hypolactasia, and thus lactose intolerance. The problem with Chagas' disease as an explanation for all Darwin's symptoms (table 2) is there is no record of Darwin on the *Beagle* having the expected initial fever and other early symptoms of Chagas' disease.²⁹ Nor does the full list of Darwin's symptoms match those of Chagas' disease. There had to be something else.

Several authors have argued strongly for a psychosomatic cause (table 1). Bolby devotes an entire book to it, arguing that the loss of his mother at the age of 8 left Darwin with severe psychological problems and a bereavement syndrome. But examination of the timing of Darwin's episodes of ill health show that they do not correlate with dates that coincide with memories of his mother. Furthermore, none of the psychosomatic hypotheses explain how such severe physiological problems, and an extraordinary diverse set of symptoms, could have a wholly psychological origin. None explain why they would suddenly remit, and then inexplicably flare up again. These ups and downs did not correlate with stress events in Darwin's life, as has often been claimed. It is striking that many of our patients, whom we have now diagnosed with systemic lactose intolerance,¹⁸ were also labelled as having a psychological problem after years of failure to find an organic cause.

EVIDENCE FOR DARWIN HAVING SYSTEMIC LACTOSE INTOLERANCE

Any explanation for Darwin's illness needs to overcome four problems;

Table 2 Systemic lactose intolerance compared with Darwin's disease

Symptoms of systemic lactose intolerance	% People with lactose intolerance who have this symptom*	Darwin's description of his symptoms	Occurrence of Darwin's symptoms
Gut symptoms (pain, bloating, diarrhoea)	100	Stomach ache	Common
Flatulence	100	Flatulence (belching)	Common
Headache	86	Headache	Common
Light headedness and loss of concentration	82	Swimming head and difficulty to concentrate	Common
Nausea and vomiting	78	Vomiting	Very common
Muscle and joint pain	71	Rheumatic pain	Often
Tiredness and chronic fatigue	63	Chronic fatigue and exhaustion	Very common
Allergy (eczema, hay fever, rhinitis, sinusitis)	40	Skin rash and boils	Often
Mouth ulcers	30	Mouth sores	Common
Heart palpitations	24	Palpitations in the chest	Common
Depression	Common, but not quantified	Depression	Frequent

*Represents proportion of people diagnosed as lactose intolerant who have this particular symptom within 48 hours of taking lactose. Darwin's occurrence is based on his notes and letters during periods of the episodes. The systemic symptoms of lactose intolerance are described previously.^{17 18}

- The wide range of organs involved (gut, heart, brain, muscles, joints, immune system).
- There was no obvious trigger setting off an episode.
- The intermittent nature of the symptoms.
- The success of the hydrotherapy treatment Darwin took from Dr Gully in Malvern.

The solution can be found in his following quotes^{1 2 27}; "The sickness starts usually about two hours after a meal"; "At no time must I take any sugar, butter, spices, tea, bacon, or anything good"; "Thank, also, my Father for his medical advice—I have been very well since Friday, nearly as well as during the first fortnight & am in heart again about the non-sugar plan." Darwin had the syndrome we described previously^{17 18}—systemic lactose intolerance.

It is clear from Darwin's autobiography,^{1 2} and the letters edited by his son Francis,²⁷ that Darwin had suffered some of the symptoms that devastated his life after marriage since childhood. There is also much evidence of family history. Emma was his first cousin and suffered bad headaches. Her uncle, Tom Wedgwood, died at the age of 34 of opium addiction, developed as a result of his friendship with Coleridge. But Wedgwood also suffered from chronic fatigue like Darwin. Darwin's elder brother Erasmus (1804–1881) never worked, and always suffered from ill health. Gwen Raverat, Darwin's grand daughter, in her book *Period Piece*²⁸ notes the "well known ill health" of the Darwin tribe. In 1841 Darwin comments, in a letter to his great friend Fox, that his sister Susan was flourishing and in good health, and that this was amazing for a Darwin. The clear implication was that the Darwins were well known for general ill health. Many of Darwin's children exhibited several of their father's symptoms. Francis describes hot and cold attacks, and his sister Annie died at the age of 9.^{29 30}

Smith^{15 16} argues that Darwin had a wide ranging, multiple allergy problem stemming from a generally weak immune system. She argues that "allergy" should mean "individual sensitivity to normally harmless substances" based on the original use by Clement von Pirquet in 1906. When we use the word allergy in medicine today the implication is that there is an antibody, usually IgE or IgG, somewhere involved in the allergic reaction. But Smith argues that cell based immune reactions do not necessarily require an antibody-antigen reaction. It is known that the gut has more immune cells than the whole of the blood, and that a range of antibody-antigen reactions occur in the gut. While Darwin's symptoms fit with general food intolerance,³¹ they do not fit in their timing and with the extent

of the recognised symptoms of allergy to food, for example, coeliac disease. The key to understanding any illness is to define the precise cellular and molecular reactions responsible for the symptoms. To be an allergy there has to be an antibody-antigen reaction. A solely cell based apparent "allergic" response involving lymphocytes would be designated as an "immune disease", but not an "allergy". This is because an allergy must generate immune complexes that excite mast cells, phagocytes and other cells to release inflammatory substances such as histamine, oxygen metabolites, and proteases. It is the release of these toxic agents that give rise locally to rashes and pain. In contrast, food intolerance entails the generation of toxins from a source other than the immune system. We propose that lactose intolerance arises from toxins generated by bacteria in the large intestine, and possibly by lactose itself.^{17 18} The timing and extent of Darwin's symptoms fit exactly those we have identified in systemic lactose intolerance (table 2).

The symptoms of lactose intolerance are the result of unabsorbed lactose, and other sugars, reaching the bacteria in the large intestine, where, under the comparatively hypoxic conditions, the hydrogen equivalents are lost as hydrogen gas (flatulence), and a variety of small organic molecules.^{17 18} It takes about two hours for food to reach the large intestine, the precise time Darwin reported it took for him to be sick after a meal. Vomiting is caused by ileus, resulting in reflux back into the stomach. Darwin admitted to a "sweet tooth". He regularly ate puddings with custard, and white sauces were common with vegetables. No medical treatment alleviated Darwin's distress. The only time he got better was after a drastic dietary change. Dr Clark took him off "much sugar",⁷ so no custard. A notable success was the water therapy of Dr Gully at Malvern.^{1 2 7 27} Hydrotherapy entailed not only cold water bathing but also drinking large amounts of water, thus reducing milk intake. Darwin comments that Dr Gully permitted him a small amount of milk on one occasion, clearly implying that the Gully therapy normally meant no milk. Darwin would have had little or no fresh milk on the *Beagle*. The cookbook of Emma his wife, with some 120 recipes, kept in the university library in Cambridge, confirms his sweet tooth and the love of rich food. Half of the recipes are desserts, with large numbers of egg yolks and cream. Emma would also have followed family advice passed down from their deceased grandfather, Dr Erasmus Darwin. Bread and milk was a typical nightcap for invalids in those days. Tragic Annie³⁰ reports a family recipe for ill people; "If you boil castor oil with an equal quantity of milk, sweeten with a little sugar, and stir well and give it

cold, children will never suspect it to be medicine, but will like it almost as well as custard".

Darwin's stress and depression have often confused the analysis of his organic symptoms. Like many creative thinkers he had his ups and downs, and was not particularly good at handling stressful situations. These could be expected to give any such person frequent indigestion. But the range of such severe physical symptoms must have had an organic cause. Anyone who suffered from these for 40 years would be expected to be depressed. Many of our 300 patients who have suffered from systemic lactose intolerance¹⁸ admit to depression, sometimes so severe that they have been referred to a psychiatrist.

Lactose intolerance is caused by loss of the enzyme lactase. There are three mechanisms:

- Congenital loss (rare)
- Inherited loss after weaning (very common)
- Reversible loss caused by gut infections or hormonal imbalance.

Genetically inherited loss is an autosomal recessive trait, and occurs in at least 8% of white northern Europeans. As many Darwins and Wedgwoods had similar problems to Charles, including his children, this family history is consistent with an inherited loss of lactase. But there is the additional possibility that this could have been compounded in Darwin's case by a secondary loss resulting for example from a gut protozoal infection such as Chagas' disease.

CONCLUSIONS

Darwin's disease is consistent with gut and systemic symptoms arising from inherited hypolactasia, with a gut infection, such as Chagas' disease, exacerbating this. The evidence supporting this hypothesis is:

- Darwin's symptoms match exactly systemic lactose intolerance (table 2; Matthews *et al*¹⁸).
- The timing of the vomiting and gut problems of two to three hours after a meal match lactose reaching the large intestine.
- Emma's cooking included a lot of desserts with cream.
- The family history shows that his problem had an inherited component, as with genetically predisposed hypolactasia.
- Darwin got better when, by chance, he reduced his milk and cream intake.
- There has been no convincing explanation until now.

What we need now is a blood spot, a hair, or even a swab off a document for some skin, so that we can carry out the DNA test to see if Darwin was CC/GG or CT/GA.¹⁸

Neither Charles Darwin nor his doctor father Robert considered the possibility of a food intolerance, and the term irritable bowel syndrome is a comparatively recent medical label. Despite Hippocrates' first description over 2000 years ago, lactose intolerance was not known in the medical literature until the 20th century. But Darwin missed something else,¹⁷ which perhaps he should have thought more about in relation to his and Wallace's principle of natural selection.^{32 33} Darwin missed the key evolutionary event that led to the origin of mammals and thus ourselves—the production of milk. Lactose is only found in mammalian milk, and lactase is unrelated to β -galactosidase in gut bacteria. So how did lactose and lactase evolve? As dairying is only some 6–8000 years old,³⁴ what could be the selective advantage of retaining any lactase after weaning? Darwin does not mention this in *The Origin of Species*³² or *The Descent of Man*.³³ Darwin insisted "Nature makes no leaps". Yet Darwin's illness highlights one of the great challenges for contemporary biology and medicine—how a

graded change occurring sometimes over millions years can lead to a rubicon, only after which is the new process susceptible to the forces of natural selection.³⁵

Darwin died just before 4 pm on 19 April 1882, not of his lifetime illness but apparently of a heart attack. Surprisingly no one seems to have considered whether he might have had a perforated peptic ulcer that would explain the severe pain and haematemesis he had at the time of death.²⁹ The study of lactose can lead to the ultimate dream he never fully addressed—the origin, as compared with the development, of species.

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